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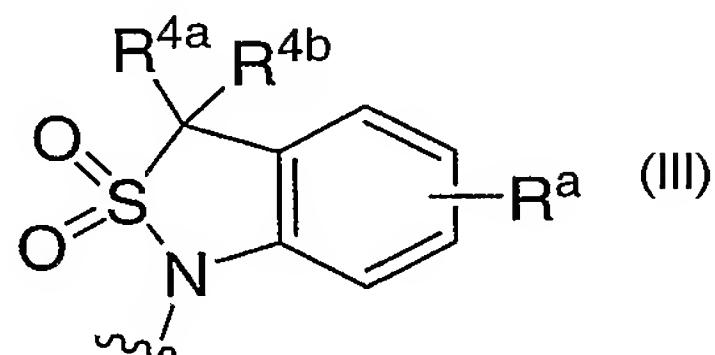
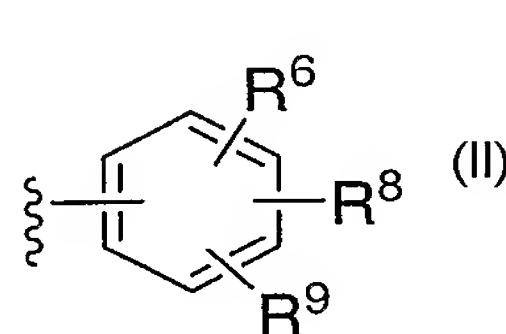
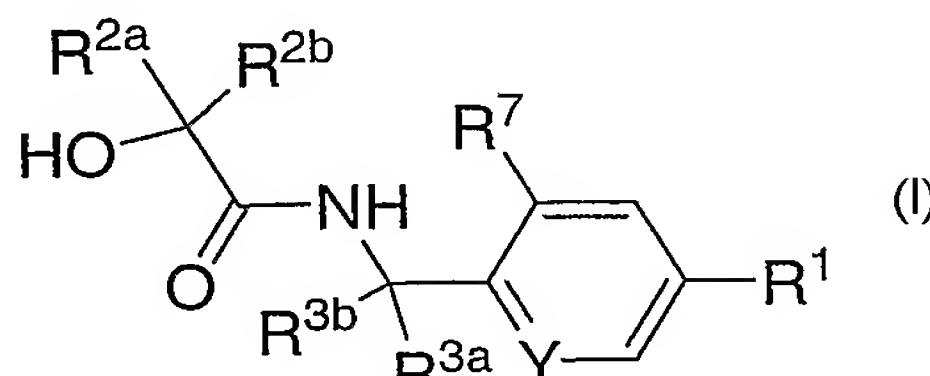
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(71) Applicant (for all designated States except US): **MERCK & CO., INC.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **WOOD, Michael, R.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **ANTHONY, Neville, J.** [GB/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **BOCK, Mark, G.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **KUDUK, Scott, D.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

(54) Title: ALPHA-HYDROXY AMIDES AS BRADYKININ ANTAGONISTS OR INVERSE AGONISTS



(74) Common Representative: **MERCK & CO., INC.**; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

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(57) Abstract:  $\alpha$ -Hydroxy amide derivatives of the general formula (I) are bradykinin B1 antagonists or inverse agonists useful in the treatment or prevention of symptoms such as pain and inflammation associated with the bradykinin B1 pathway. R<sup>2a</sup> is selected from (1) a group selected from R<sup>a</sup>. (2) (CH<sub>2</sub>)<sub>n</sub>NR<sup>b</sup>C(O)R<sup>a</sup>. (3)(CH<sub>2</sub>)<sub>n</sub>NR<sup>b</sup>SO<sub>2</sub>R<sup>d</sup>. (4)(CH<sub>2</sub>)<sub>n</sub>NR<sup>b</sup>CO<sub>2</sub>R<sup>a</sup>. (5)(CH<sub>2</sub>)<sub>k</sub>-heterocycle optionally substituted with 1 to 3 groups independently selected from halogen, nitro, cyano, OR<sup>a</sup>, SR<sup>a</sup>, C<sub>1-4</sub> alkyl and C<sub>1-3</sub> haloalkyl wherein said heterocycle is (a) a 5-membered heteroaromatic ring having a ring heteroatom selected from N, O and S, and optionally having up to 3 additional ring nitrogen atoms wherein said ring is optionally benzo-fused; or (b) a 6-membered heteroaromatic ring containing from 1 to 3 ring nitrogen atoms and N-oxides thereof. Wherein said ring is optionally benzo-fused. (6)(CH<sub>2</sub>)<sub>k</sub>CO<sub>2</sub>R<sup>a</sup>. and (7)(CH<sub>2</sub>)<sub>n</sub>C(O)NR<sup>b</sup>R<sup>c</sup>. R<sup>2b</sup> is OH or a group selected from R<sup>2a</sup>; or R<sup>2a</sup> and R<sup>2b</sup> together with the carbon atom to which they are attached form a 3-to 7-membered carbocyclic ring optionally substituted with 1 to 4 groups independently selected from halogen, OR<sup>a</sup>, C<sub>1-4</sub> alkyl and C<sub>1-4</sub> haloalkyl;

N-oxides thereof. Wherein said ring is optionally benzo-fused. (6)(CH<sub>2</sub>)<sub>k</sub>CO<sub>2</sub>R<sup>a</sup>. and (7)(CH<sub>2</sub>)<sub>n</sub>C(O)NR<sup>b</sup>R<sup>c</sup>. R<sup>2b</sup> is OH or a group selected from R<sup>2a</sup>; or R<sup>2a</sup> and R<sup>2b</sup> together with the carbon atom to which they are attached form a 3-to 7-membered carbocyclic ring optionally substituted with 1 to 4 groups independently selected from halogen, OR<sup>a</sup>, C<sub>1-4</sub> alkyl and C<sub>1-4</sub> haloalkyl;